REMARKS

Applicants request reconsideration of the outstanding rejections in view of the comments set forth herein and in the Amendment And Response Pursuant to 37 C.F.R. § 1.111, filed December 20, 2002, said comments being incorporated by reference in their entirety herein.

Objections to the Drawings

The Examiner again objects to the drawings for reasons that were supposed to be indicated on an accompanying PTO Form 948. The Examiner indicates that corrected drawings are required and that this objection will not be held in abeyance. However, the copy of PTO Form 948 that Applicants received with the Advisory Action of November 19, 2003 is not legible. Applicants respectfully request another copy of the form.

Rejections under 35 U.S.C. § 112, ¶ 1: Written Description

Claims 6-9, 11-14, and 16-23 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors were in possession of the claimed invention at the time the application was filed. The Examiner asserts that neither the specification nor the prior art describe the sequence of genes encoding endocelluases, exocelluases, or cellobioses to the full breadth of the claims. Applicants respectfully traverse this rejection.

As pointed out in the previous response, § 112, first paragraph does not require a description of all other DNA molecules encoding cellulases encompassed by the claims. Nor does it require a description of the structural features that distinguish all such nucleic acids from other nucleic acids. At most, the law requires a description of a representative number of species.

The claimed invention is directed to "[a] transgenic plant comprising a nucleic acid encoding a cellulase" and a transgenic seed obtained therefrom, not to "a nucleic acid encoding a cellulase" *per se*. Therefore, the written description needs to be specific enough to lead the skilled artisan to the class of DNA molecules that encode cellulases. *In re Herschler*, 591 F.2d 693, 702 ("claims drawn to the use of known chemical

compounds in a manner auxiliary to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds.") Moreover, as the Office has indicated, a proper determination of whether the written description requirement is satisfied necessitates a reading of the disclosure in the light of the knowledge possessed by those of skill in the art at the time of filing. MPEP § 2163 II.A.2.

Applicants reiterate that the specification more than satisfies the written description requirements of § 112, first paragraph. For example, as previously pointed out, the specification teaches T. *fusca* E1, E2, E4, and E5 genes. Specifically, the specification states,

> The *T. fusca* genes that encode cellulose-degrading enzymes have been cloned and extensively characterized. (*See, e.g.,* Collmer *et al.* (1983) Bio/Technology 1:594-601, hereby incorporated by reference; Ghangas *et al.* (1988) Appl. Environ. Microbiol. 54:2521-2526, hereby incorporated by reference; and Wilson (1992) Crit. Rev. Biotechnol. 12:45-63, hereby incorporated by reference). In addition, the DNA sequences of a cellobiohydrolase gene and an endoglucanase gene from *T. fusca* have been determined (Jung *et al.* (1993) Appl. Environ. Microbiol. 59:3032-3043, hereby incorporated by reference); and the DNA sequences of three endoglucanase genes from *T. fusca* have also been determined (Lao *et al.* (1991) J. Bacteriol. 173:3397-3407, hereby incorporated by reference)....

Specification, p. 4, ¶ 1.

Contrary to the Examiner's assertion, while Collmer does describe an endocellulase gene from *Thermomonospora. YX*, the reference **also** teaches that Whittle et al. cloned a cellulase gene from *Cellulomonas fimi* and that Cornet et al. cloned a thermophilic cellulase gene from *Clostridium Thermocellum.* (See 595, left hand column, third paragraph.)

As Applicants additionally pointed out previously, a variety of other exemplary genes are taught in the specification, including, for example, a *B. subtilis* endoglucanase and a *C. fimi* β-D-glucosidase (Yoo *et al.* (1992) Biotechnol. Lett. 14:77-82), as well as several cellulases that have been expressed from heterologous systems and have been reported in the literature (see Thomas *et al.*, "Initial Approaches to Artificial Cellulase

Systems for Conversion of Biomass to Ethanol" in *Enzymatic Degradation of Insoluble Carbohydrates*, J.N. Saddler and M.H. Penner, eds., ACS Symposium Series 618:208-36, 1995, American Chemical Society, Washington, D.C., Table II, pp. 214-216 (enclosed herewith as Exhibit A). As described in the specification, these exemplary cellulases include, but are not limited to, endoglucanases, exoglucanases, and β-D-glucosidases derived from microorganisms such as bacteria and fungi. See Specification, paragraph bridging pp. 14 and 15.

In addition, the specification provides examples that describe, in detail, plants that express *T. fusca* sequences encoding two β-1,4-endoglucanases (*i.e.*, *T. fusca* E1 and E5) as well as a cellobiohydrolase (*i.e.*, *T. fusca* E2). See Specification at, *inter alia,* pp. 39-45 (Examples A1 through A11)

Applicants therefore reiterate that the specification reasonably conveys that Applicants were in possession of the claimed invention at the time the application was filed. Not only does the specification provide sufficient teaching to clearly lead the skilled artisan to the relevant class of nucleic acids (*i.e.*, those encoding cellulases) to be transformed into a plant in accordance with the claimed invention, but it more than adequately describes a representative number of species within that class (*i.e.*, DNA molecules encoding: endocellulases, such as β-1,4-endoglucanases; exocellulases, such as cellobiohydrolases; and cellobioses, such as 1,4- β-D-glucosidases).

For the reasons set forth above, Applicants submit that the instant application provides sufficient written description support for the claimed invention, *i.e.*, a transgenic plant comprising a nucleic acid encoding a cellulase and a transgenic seed obtained therefrom. The law requires no more. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. § 112, ¶ 1: Enablement

Claims 6-9, 11-14, and 16-23 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. The Examiner contends that neither the specification nor the prior art describe the sequence of genes encoding

endocelluases, exocelluases, or cellobioses to the full breadth of the claims. Applicants respectfully traverse this rejection.

The Examiner asserts that Applicants' previous arguments are not persuasive because page 4 of the specification (Collmer et al., Ghanges et al., Wilson, and Lao) teaches *T. fusca* cellulases. Applicants respectfully disagree. As pointed out above the cited references teach a variety of genes encoding cellulases, not just genes from *T. fusca*. For example, Collmer teaches an endocellulase gene from *Thermomonospora. YX*, and **also** teaches that Whittle et al. cloned a cellulase gene from *Cellulomonas fimi* and that Cornet et al. cloned a thermophilic cellulase gene from *Clostridium Thermocellum*. (See 595, left hand column, third paragraph.)

The Examiner further asserts that it's only Thomas et al. that discusses cellulases from other organisms and that the reference only addresses enzymes. Applicants respectfully direct the Examiner's attention to Table II, pages 214-216 of Thomas et al., which provides a list of genes encoding cellulases from a variety of organisms.

Hence, contrary to the Examiner's allegations, the instant disclosure provides sufficient guidance and direction to enable the practice of the claimed invention without undue experimentation. As discussed above, the specification provides considerable guidance and direction regarding the class of cellulases that may be expressed in a plant in accordance with the claimed invention. In particular, the specification describes various cellulases that have been cloned, characterized, and/or heteologously expressed in bacterial hosts. These described cellulases include endocellulases (*e.g.*, β-1,4-endoglucanases); exocellulases (*e.g.*, cellobiohydrolases); and cellobioses (*e.g.*, 1,4- β-D-glucosidases). See, *e.g.*, Specification, p. 4, ¶¶ 1 and 2; and paragraph bridging pp. 14 and 15 (as quoted above).

The Examiner contends that the specification as well as the cited art, other than Thomas, are limited to teachings of T. fusca. For the reasons set forth above, Applicants respectfully disagree.

Applicants submit that the disclosure provides more than a reasonable amount of guidance and direction for using the disclosed means to express a cellulase in a plant.

In addition to providing numerous references that disclose various cellulase genes (see, *e.g.*, Specification, pp. 14-15), the specification provides detailed guidance regarding the modification of microbial genes to optimize nuclear expression of those genes in plants. Specification, pp. 15-18. There is also guidance and direction regarding the construction of plant transformation vectors (Specification, pp. 18-21) as well as the construction of plant expression cassettes (Specification, pp. 21-24), including examples of expression cassette construction and a detailed discussion of various plant expressible promoters that may be employed in the practice of the invention (Specification, pp. 24-33). The specification also provides guidance regarding the transformation of both dicotyledons and monocotyledons (Specification, pp. 33-36), as well as plastid transformation techniques (Specification, pp. 36-38).

Moreover, the specification discloses numerous working examples of various means for expressing cellulase in a plant. There are several examples of the preparation of constructs containing various cellulase coding sequences (*i.e.*, *T. fusca* E1, E2, and E5), each fused either to an inducible or constitutive plant expressible promoter (*i.e.*, tobacco PR-1a or CaMV 35S, respectively) (Examples A1-A6). There are examples of the transformation of various monocot and dicot plants (*i.e.*, tobacco, maize, and wheat) with the disclosed cellulase constructs (Examples A7-A9). There are examples regarding the vacuole-targeted expression of cellulases (Examples B1-B13). There are also examples of chloroplast expression of cellulase genes (Examples C1-C13).

Applicants respectfully submit that the working examples, in conjunction with the remainder of the disclosure, provide sufficient guidance and direction to enable one skilled in the art to practice the claimed invention employing no more than routine experimentation. Specifically, in view of the advanced state of the transformation art as of the filing date of the instant application and the specification's detailed guidance and direction regarding the transformation of plants to achieve the expression of cellulase, a skilled artisan would have been able to transform a plant with any of a variety of known cellulase genes employing no more than routine experimentation.

Applicants respectfully reiterate that "[e]nablement is not precluded by the necessity for some experimentation such as routine screening." *In re Wands*, 858 F.2d

731, 736-737 (Fed. Cir. 1988). In fact, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *Id.* at 737 (internal citation omitted). The instant specification provides such guidance, via general teachings and more detailed examples. Practicing non-exemplified embodiments of the claimed invention would have required the routine preparation of vector constructs, in accordance with the teachings of the disclosure, and limited and systematic routine screening of, for example, plants transformed to express the various disclosed species within the described genus of cellulase genes. Applicants respectfully submit that, even where required, such efforts do not rise to the level of undue experimentation.

For the foregoing reasons, Applicants respectfully submit that the instant specification, coupled with what was known in the art at the time of filing, would have provided sufficient guidance to enable one of ordinary skill in the art to practice the claimed invention without undue experimentation. Accordingly, the claimed invention is enabled, and Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. § 103: Bennett

Claims 6-8, 16-18, and 21-23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bennett *et al.*, U.S. Patent No. 5,168,064, issued December 1, 1992 ("the '064 Patent").

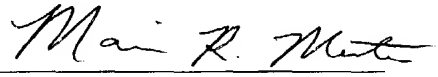
Applicants reiterate that two of the inventors (*i.e.*, Bennett and Lashbrook) of the '064 Patent are also authors of the later published Lashbrook reference cited by the Examiner and discussed in detail above. Further, the amino acid sequence of the endo-β-1,4-glucanase disclosed in Table I of the '064 Patent is the same sequence later identified in Lashbrook as the endo-β-1,4-glucanase Cel 1 (see Figure 1). Thus, as discussed previously, and by the inventors' own admission, the endo-β-1,4-glucanase disclosed in the '064 Patent is not a cellulase. As the inventors state, "[a]lthough the term 'cellulase' has been widely used to describe these endoglucanases, the term is misleading in view of the current lack of evidence for EGase-catalyzed cellulose

degradation." Lashbrook, p. 1486. Further, "the nature of the cell wall substrate(s) modified by these enzymes [*i.e.*, endoglucanases expressed in tomato plants during fruit ripening] and thus their physiological function are unknown." *Id.* Thus, the reference cited by the Examiner does not teach or suggest all of the claim elements. The Examiner stated that this argument was not deemed persuasive because the specification teaches that endo-beta-1,4 glucanases are cellulases. Applicants respectfully submit that the statements in Lashbrook indicate the the specific endoglucanases are not cellulases. The relevant inquiry is whether Lashbrook teaches or suggests Applicants' claimed invention. Whether the instant specification teaches that 1,4 endoglucanases are cellulases is not at issue.

For the reasons set forth above, Applicants submit that the '064 Patent does not render Claims 6-8, 16-18, and 21-23 obvious. Accordingly, the claims are patentable over the reference, and Applicants respectfully request reconsideration and withdrawal of this rejection under 35 U.S.C. § 103(a).

Pursuant to the foregoing remarks, Applicants respectfully submits that all of the pending claims fully comply with 35 U.S.C. § 112 and are allowable over the prior art of record. Reconsideration of the application and allowance of all pending claims is earnestly solicited. Should the Examiner wish to discuss any of the above in greater detail or deem that further amendments should be made to improve the form of the claims, then the Examiner is invited to telephone the undersigned at the Examiner's convenience.

Respectfully submitted,



Marcia R. Morton
Attorney for Applicants
Registration No. 46,942

Syngenta Biotechnology, Inc.
P.O. Box 12257
Research Triangle Park, NC 27709-2257
Telephone: 919-541-8566
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